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| APPLICATION NO.                                                                                                                                                                                   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO.                                  | CONFIRMATION NO.                               |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|----------------------|------------------------------------------------------|------------------------------------------------|
| 10/814,232                                                                                                                                                                                        | 04/01/2004  | Kei Takenaka         | 500.43725X00                                         | 5361                                           |
| <div>20457      7590      07/12/2007</div> <div>ANTONELLI, TERRY, STOUT &amp; KRAUS, LLP</div> <div>1300 NORTH SEVENTEENTH STREET</div> <div>SUITE 1800</div> <div>ARLINGTON, VA 22209-3873</div> |             |                      |                                                      |                                                |
|                                                                                                                                                                                                   |             |                      | <div>EXAMINER</div> <div>BOWERS, NATHAN ANDREW</div> |                                                |
|                                                                                                                                                                                                   |             |                      | <div>ART UNIT</div> <div>1744</div>                  | <div>PAPER NUMBER</div>                        |
|                                                                                                                                                                                                   |             |                      | <div>NOTIFICATION DATE</div> <div>07/12/2007</div>   | <div>DELIVERY MODE</div> <div>ELECTRONIC</div> |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

officeaction@antonelli.com  
dprater@antonelli.com  
tsampson@antonelli.com

|                              |                               |                                 |  |
|------------------------------|-------------------------------|---------------------------------|--|
| <b>Office Action Summary</b> | Application No.<br>10/814,232 | Applicant(s)<br>TAKENAKA ET AL. |  |
|                              | Examiner<br>Nathan A. Bowers  | Art Unit<br>1744                |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 01 April 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 01 April 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>102805</u> .                                                  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

- 1) Claim 9 is rejected under 35 U.S.C. 102(b) as being anticipated by Franzen (US 6180372).

Franzen discloses a nucleic acid amplifying method comprising a branch step for branching a reaction fluid containing a sample of nucleic acid and reagent. Column 8, lines 29-49 state that a flow passage includes a branch portion (Figure 2:2) that creates a plurality of parallel fluid passages (Figure 2:3). Column 6, lines 30-52 and column 8, line 29 to column 9, line 2 indicate that the branched reaction fluid parts are repeatedly heated and cooled at a plurality of different temperatures.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

- 2) Claims 1, 2, 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Fouillet (US 20060011478).

With respect to claims 1, 2 and 7, Franzen discloses a nucleic acid amplifying apparatus comprising a flow passage through which a reaction fluid containing a nucleic acid and a reagent flows. The flow passage includes a flow passage branch portion (Figure 2:2) at which the flow passage branches into a plurality of branch flow passages (Figure 2:3). A junction portion (Figure 2:4) is also provided at which the plurality of flow

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passages join. This is described in column 8, line 29 to column 9, line 2. Column 6, lines 30-52 state that a heating mechanism is provided to cycle the fluid moving through the branch flow passages through a plurality of different temperatures. Franzen, however, teaches that a heating element is used to produce different temperatures over time. Franzen does not expressly disclose a plurality of set temperature zones provided by a first and second heating mechanism.

Fouillet discloses a thermal cycling device capable of amplifying nucleic acid samples via PCR. Paragraph [0205] indicates that a flow passage (Figure 12:1) is provided such that fluids are repeatedly passed through a plurality of zones (Figure 12:4,5,6) heated by different heating mechanisms.

Franzen and Fouillet are analogous art because they are from the same field of endeavor regarding thermal cycling apparatuses.

At the time of the invention, it would have been obvious to replace the programmable heating mechanisms of Franzen with a plurality of heating elements maintained at a set temperature. In Figure 12, Fouillet teaches that it is known in the art to repeatedly move fluids across several heating areas in order to produce a temperature change in the nucleic acid solution. One of ordinary skill in the art would recognize that the use of first and second heating mechanisms maintained at steady temperatures would offer a viable and effective alternative to the use of a single heating mechanism that is cycled between two temperatures. Moving a nucleic acid sample repeatedly across a several set heating regions in order to affect temperature change in the fluid is considered to be well known in the art.

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With respect to claim 8, Franzen and Fouillet disclose the combination as previously described above. In addition, Fouillet indicates in paragraph [0128] that it is known to provide microfluidic thermal cycling devices with an integrated detection system capable of detecting a desired product. At the time of the invention, it would have been obvious to ensure that the system of Franzen is provided with a detection part that detects the nucleic acid in the reaction fluid following and/or during thermal cycling. In this way, the use of additional, remote detection devices would no longer be necessary, which would improve the efficiency of the operation.

3) Claims 3-6, 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Franzen (US 6180372) in view of Fouillet (US 20060011478) and Enzelberger (US 20050221373).

Franzen and Fouillet disclose the combination as previously described in the rejections above, however do not expressly disclose that the use of a second branch portion and second branch flow passages.

Enzelberger discloses a microfluidic system in which a plurality of flow passages (Figure 5:S1-S5) containing a nucleic acid solution are repeatedly split and recombined to form a grid of discrete temperature areas (Figure 5:502). This is disclosed in paragraphs [0113]-[0121]. Each temperature area represents a junction portion that produces branch flow passages. Figure 5 indicates that a plurality of junction portions are provided in order to provide thermal cycling during PCR. A plurality of additional

flow passages (Figure 5:P1-P5) are capable of delivering reagents to the reaction areas.

Franzen, Fouillet and Enzelberger are analogous art because they are from the same field of endeavor regarding microfluidic thermal cycling devices.

At the time of the invention, it would have been obvious to alter the apparatus and method set forth by Franzen and Fouillet in order to provide a second branch portion and second branch flow passages disposed downstream from the first branch portion and the first branch flow passages. Enzelberger teaches that microfluidic devices comprising multiple branching steps are well known in art. The addition of a second branch portion to Franzen's device would have been beneficial because it would have allowed the sample solution to experience extra temperature cycles capable of enhancing nucleic acid amplification. Since Franzen already discloses the use of a branch portion and branch flow passages subjected to heating, the addition of a second branch portion and second branch flow passages merely represents the duplication of parts already disclosed in the prior art. It would have been apparent to add second, third, fourth, etc branch portions to the system of Franzen to obtain the expected result of additional thermal cycling area. See MPEP 2144.04.

### ***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The Villa (US 20030057199) and Foret (US 20020157951)

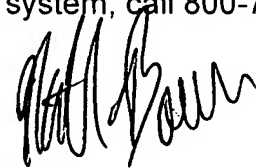
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references disclose the state of the art regarding microfluidic thermal cycling apparatuses.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



NAB

  
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SUPERVISORY PATENT EXAMINER